

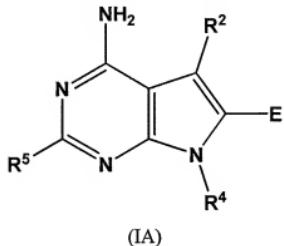
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of claims:

1. - 2. (Canceled)

3. (Currently amended) A compound having the formula (IA):



in which

R² is hydrogen or a group having the formula (CH₂)_bR^b wherein b is 0 or an integer from 1 to 3 and R^b is an aromatic, heterocyclic or cyclical aliphatic group optionally substituted with one or more groups selected from lower alkyl, halogen, substituted alkyl, nitro, alkoxy, phenoxy, sulfonamido, carboxylic ester, or carboxamide;

R⁴ is an aliphatic, aromatic, or heterocyclic group optionally substituted with one or more polar groups, which polar group may be protected or unprotected;

R⁵ is hydrogen or an alkyl- or aryl-substituted ether, thioether, or amine; and

E comprises **a carbonyl an oxo group bound to a carbon atom**, an epoxide, or an olefin conjugated to an electron withdrawing group;

provided that the compound is not a compound in which, R² is 4-phenoxyphenyl, E is cyano, R⁴ is cyclopentyl, and R⁵ is hydrogen.

4. (Canceled)

5. (Previously Presented) A compound according to claim 3 in which R² is hydrogen.

6. (Previously Presented) A compound according to claim in which R² is a group having the formula (CH₂)_bR^b.

7. (Original) A compound according to claim 6 in which b is 0.

8. (Original) A compound according to claim 7 in which R² is an optionally substituted phenyl group.

9. (Canceled)

10. (Currently amended) A compound according to claim 3 in which E ~~comprises is~~ an olefin conjugated to a carbonyl, nitro, cyano, carboxyl, carboxamide, sulfoxide, sulfonyl, sulfonamide, or sulfonate group.

11. (Currently amended) A compound according to claim 3 in which E comprises ~~a carbonyl an oxo group bound to a carbon atom~~.

12. (Previously Presented) A compound according to claim 11 in which E has the formula -C(O)(CH₂)_nR in which R is a halogen and n is 0 or an integer from 1 to 6.

13. (Original) A compound according to claim 12 in which n is 0.

14. (Original) A compound according to claim 12 in which n is 1.

15. (Previously Presented) A compound according to claim 11 in which E has the formula -(CH₂)_mC(O)R in which m is 0 or an integer from 1 to 6 and R is a halogen.

16. (Original) A compound according to claim 15 in which m is 0.

17. (Original) A compound according to claim 15 in which m is 1.

18. (Original) A compound according to any of claims 12-17 in which R is chloro.

19. (Original) A compound according to any of claims 12-17 in which R is fluoro.

20. (Previously Presented) A compound according to claim 11 in which E comprises an olefinically unsaturated ketone.

21. (Previously Presented) A compound according to claim 20 in which E is -C(O)CH=CH₂.

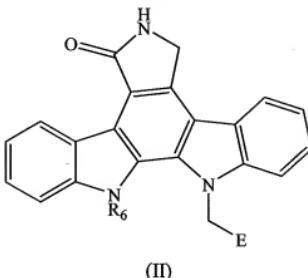
22. (Previously Presented) A compound according to claim 3 in which E is an olefin carboxylate having the formula CH=CHC(O)OR' where R' is an optionally substituted aliphatic, aromatic, or heterocyclic moiety.

23. (Original) A compound according to claim 22 in which R' is methyl.

24. (Previously Presented) A compound according to claim 3 in which E is an olefin carboxamide having the formula -CH=C(O)NR'R" where R' and R" are optionally substituted aliphatic, aromatic, or heterocyclic moieties.

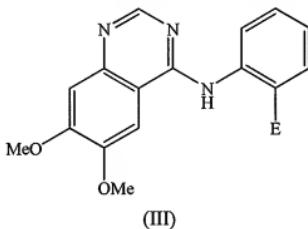
25. (Previously Presented) A compound according to claim 3 in which E comprises an epoxide.

26. (Withdrawn) A compound having the formula (II):



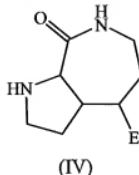
in which R_6 is hydrogen or an optionally substituted aliphatic, aromatic or heterocyclic group and E represents an electrophilic group that is capable of reacting with a cysteine residue within the ATP binding site of a kinase.

27. (Withdrawn) A compound having the formula (III):



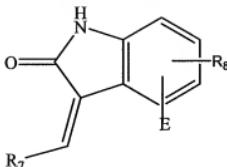
in which E represents an electrophilic group that is capable of reacting with a cysteine residue within the ATP binding site of a kinase.

28. (Withdrawn) A compound having the formula (IV):



in which E represents an electrophilic group that is capable of reacting with a cysteine residue within the ATP binding site of a kinase.

29. (Withdrawn) A compound having the formula (V):



(V)

in which R₇ is a group having the formula (CH₂)_bR^b wherein b is 0 or an integer from 1 to 3 and R^b is an aromatic, heterocyclic or cyclical aliphatic group; R₈ is hydrogen or one or more substituents that do not affect the kinase-inhibiting properties of the said compounds, and E represents an electrophilic group that is capable of reacting with a cysteine residue within the ATP binding site of a kinase.

30. (Withdrawn) A compound according to any of claims 26-29 in which E comprises a carbonyl, an epoxide, or an olefin conjugated to an electron withdrawing group.

31. (Withdrawn) A compound according to any of claims 26-29 in which E comprises an olefin conjugated to a carbonyl, nitro, cyano, carboxyl, carboxamide, sulfoxide, sulfonyl, sulfonamide, or sulfonate group.

32. (Withdrawn) A compound according to any of claims 26-29 in which E comprises a carbonyl group.

33. (Withdrawn) A compound according to claim 32 in which the carbonyl group has the formula -C(O)(CH₂)_nR in which R is a halogen and n is 0 or an integer from 1 to 6.

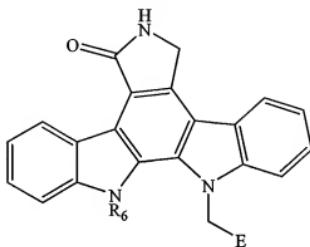
34. (Withdrawn) A compound according to claim 33 in which n is 0.

35. (Withdrawn) A compound according to claim 33 in which n is 1.

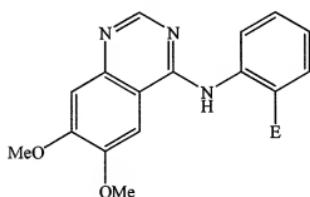
36. (Withdrawn) A compound according to claim 32 in which the carbonyl group has the formula -(CH₂)_mC(O)R in which m is 0 or an integer from 1 to 6 and R is a halogen.

37. (Withdrawn) A compound according to claim 36 in which m is 0.
38. (Withdrawn) A compound according to claim 36 in which m is 1.
39. (Withdrawn) A compound according to any of claims 33-38 in which R is chloro.
40. (Withdrawn) A compound according to any of claims 33-38 in which R is fluoro.
41. (Withdrawn) A compound according to claim 32 in which the carbonyl group comprises an olefinically unsaturated ketone.
42. (Withdrawn) A compound according to claim 41 in which the carbonyl group is $-\text{C}(\text{O})\text{CH}=\text{CH}_2$.
43. (Withdrawn) A compound according to any of claims 26-29 in which E is an olefin carboxylate having the formula $\text{CH}=\text{CHC}(\text{O})\text{OR}'$ where R' is an optionally substituted aliphatic, aromatic, or heterocyclic moiety.
44. (Withdrawn) A compound according to claim 43 in which R' is methyl.
45. (Withdrawn) A compound according to any of claims 26-29 in which E is an olefin carboxamide having the formula $-\text{CH}=\text{C}(\text{O})\text{NR}''\text{R}'''$ where R'' and R''' are optionally substituted aliphatic, aromatic, or heterocyclic moieties.
46. (Withdrawn) A compound according to any of claims 26-29 in which E comprises an epoxide.
47. (Previously Presented) A method of inhibiting a protein kinase that has one or more cysteine residues within its ATP binding site, comprising contacting the kinase with an inhibitory-effective amount of a compound according to claim 3.
48. - 49. (Canceled)

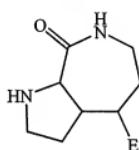
50. (Withdrawn) A method of inhibiting a protein kinase that has one or more cysteine residues within its ATP binding site, comprising contacting the kinase with an inhibitory-effective amount of a compound having the formula (II), (III), (IV) or (V):



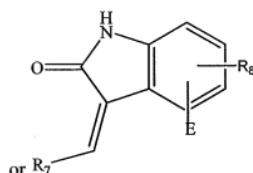
(II)



(III)



(IV)



(V)

in which R₆ is an optionally substituted aliphatic, aromatic or heterocyclic group; R₇ is a group having the formula (CH₂)_bR^b wherein b is 0 or an integer from 1 to 3 and R^b is an optionally

substituted aromatic, heterocyclic or cyclical aliphatic group; R₈ is hydrogen or one or more substituents that do not affect the kinase-inhibiting properties of the said compounds, and E represents an electrophilic group that is capable of forming a covalent bond with a cysteine residue within the ATP binding site of a kinase.

51. (Previously Presented) A method of imparting to a protein kinase the capability of being inhibited by a compound according to claim 3, comprising replacing an amino acid residue other than a cysteine residue within the ATP binding site of the protein kinase with a cysteine residue.

52. (Previously Presented) A method of imparting to a protein kinase the capability of being inhibited by a compound according to claim 3, comprising replacing a methionine, leucine, isoleucine, lysine, arginine, tryptophan, glutamine, asparagine, proline, tyrosine, histidine, glutamic acid, aspartic acid, valine, or phenylalanine residue in the gatekeeper position of the ATP binding site with a smaller residue.

53. (Previously Presented) A method for inhibiting the morphological transformation of a cell in which such a kinase is expressed comprising contacting the cell or the kinase with an inhibitory-effective amount of a compound according to claim 3.

54. (Previously Presented) A method for inhibiting the proliferation of a tumor cell comprising contacting the cell with an inhibitory-effective amount of a compound according to claim 3.

55. - 57. (Canceled)

58. (Withdrawn) A method according to claim 54 in which the compound is a compound according to any of claims 26-29.

59. (Original) A method according to claim 54 in which the cell is contacted with an inhibitory-effective amount of a plurality of such compounds.

60. (Withdrawn) An array for testing for inhibition of protein kinase activity comprising one or a plurality of compounds according to claim 3.

61. (Currently Amended) A therapeutic composition comprising [[(a)]] a kinase inhibitory-effective amount of a composition according to claim 3 and a pharmaceutically acceptable carrier.

62. (Previously Presented) A composition for inhibiting kinase activity comprising an effective inhibitory amount of a compound according to claim 3.

63. (Original) A composition according to claim 62 for inhibiting activity of a kinase selected from the group consisting of Rsk1,2,3,4, Msk1-2, Plk1-3, MEKK1, and Nek2.

64. (New) The compound according to claim 3,
in which

E is a group having the formula $-\text{C}(\text{O})\text{CH}=\text{CH}_2$, $-(\text{CH}_2)_m\text{COR}'$, $-\text{CO}(\text{CH}_2)_n\text{R}'$ or $-\text{C}(\text{O})\text{C}(\text{O})\text{R}'$,
wherein m and n are independently 0 or an integer from 1 to 6,
wherein R' is hydrogen, halogen, cyano, amino, substituted amino, alkyl,
substituted alkyl, aryl, substituted aryl, heterocyclic or substituted heterocyclic
group, and
wherein the substituted aliphatic, substituted aromatic or substituted heterocyclic
group are independently substituted with halo, hydroxyl, thiol, nitro, amino,
substituted amino, amido, substituted amido, alkoxy, haloalkoxy, alkylenedioxy,
alkyl, haloalkyl, hydroxylalkyl or sulfonyl;
an epoxide having 2 to 4 carbon atoms, or
an olefin substituted with a carbonyl, nitro, cyano, carboxyl, carboxamido, sulfoxidyl,
sulfonyl, sulfonamidyl or sulfonoyl group.

65. (New) The compound according to claim 64, wherein E is an olefin carboxylate or an olefin carboxamide.